UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/474,980	12/29/1999	Eugene M. Johnson	6029-2668	3036

21888 7590 11/06/2003

THOMPSON COBURN, LLP
ONE US BANK PLAZA
SUITE 3500
ST LOUIS, MO 63101

EXAMINER	
HAYES, ROBERT CLINTON	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 11/06/2003

17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/474,980	Johnson et al
Examiner	**Art Unit**
Robert C. Hayes, Ph.D.	1647

-- *The MAILING DATE of this communicati n appears on the cover sh et with the corresp ndence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jun 19, 2003*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under ***Ex parte Quayle***, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *32-38 and 40-59* is/are pending in the application.

4a) Of the above, claim(s) *40-59* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *32-38* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *32-38 and 40-59* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 3
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered first claim 33 has been renumbered 32.

Election/Restriction

2. Applicant's election without traverse of Group I (i.e., claims 32-38; as it relates to SEQ ID NO:221) in Paper No: 16 is acknowledged.

Claims are 40-59 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Election was made without traverse in Paper NO: 16.

Claim Rejections - 35 U.S.C. § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32-38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Although page 5 of the specification state that "mouse, rat and human mature persephin sequences show from about 80% to about 94% sequence identity", no generic persephin sequences are disclosed, nor are any persephin sequence disclosed from any different species, nor are any variants of these three species of persephin molecules described. In other words, no written description of any different functional persephin molecules that can be structurally envisioned by one skilled in the art (i.e., by amino acid sequence) is adequately disclosed within the specification by which one of ordinary skill in the art could then generate antibodies "capable of reacting with a persephin polypeptide of about 80% or greater identity to SEQ ID NO:221" that still possess the desired functional characteristics of the instant invention; thereby, not meeting the written description requirements of 35 U.S.C. 112, first paragraph.

It is noted that no distinguishable functional language in order to both structurally and functionally describe the persephin polypeptides required to generate the antibodies of the instant invention is recited in the claims.

Additionally, the specification does not disclose any assays that appear to distinguish a persephin neurotrophic factor from any different neurotrophic factor; especially as it relates to how persephin is defined on page 17 of the specification, in that the term "persephin... herein is intended to be construed to include growth factors of any origin which are substantially homologous to and which are *biologically equivalent,..* to the persephin characterized and

described herein..." [emphasis added]. In particular, the specification does not disclose any assays that appear to distinguish a persephin neurotrophic factor from any different neurotrophic factor with any given percent sequence identity, or from even different neurturin-persephin-GDNF family members, in that all these family members have the same activity of increasing survival of dopaminergic neurons.

Applicant is directed toward the Revised Interim Utility Guidelines, Federal Register, Vol.64, No.244, pages 71427-71440, Tuesday December 21, 1999. See Examples 13 & 16.

4. Claims 32-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for antibodies directed toward the human persephin polypeptide of SEQ ID NO: 221, does not reasonably provide enablement for generating antibodies against any polypeptide without sufficiently defined/distinguishable structural and functional characteristics. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The specification discloses the amino acid sequences of murine, rat and human persephin, and in general teaches on how to make polyclonal and monoclonal antibodies to such. However, Fox (U.S. Patent Number 4,879,213) sets forth that "without knowing a protein's three dimensional structure there is no reliable method for determining which linear segments of the protein are accessible to the host's immune system" and that "whether the three dimensional

structure is known or not, short linear polypeptides often appear not to have the ability to mimic the required secondary and tertiary conformational structures to constitute appropriate immunogenic and antigenic determinants" (see column 3; as it relates to claims 35-38). In other words, claims directed to generating antibodies to random "portions of the persephin polypeptide", "oligopeptides", or even "hydrophilic" "oligopeptides" without further guidance from the specification and/or distinguishable structural and functional characteristics for the persephin polypeptide itself would be expected by the skilled artisan to alternatively prevent generation of an antibody that specifically binds the native human persephin polypeptide of SEQ ID NO:221, without requiring undue experimentation to determine otherwise.

In addition, generation of any such antibodies to modified full length polypeptides without further recited and definable structural and functional characteristics would be expected by the skilled artisan to result in antibodies that no longer bind to the persephin polypeptide of SEQ ID NO: 221, or alternatively cross-react with different proteins (i.e., as it relates to claim 32). For example, Geysen et al. teach that random amino acid changes to a tetrameric peptide/ epitope, which includes conservative substitutions to the same antigen, have "frequently been associated with loss of antibody binding" (e.g., pg. 38, 1st col., 2nd *pp*). Thus, the lack of guidance provided in the specification as to what minimal structural requirements are necessary for any specific persephin antibody binding reaction would prevent the skilled artisan from determining whether any random modification or truncation to the human persephin protein sequence depicted as SEQ ID NO: 221 could be made that successfully generates the desired

antibodies of the instant invention, because any random modification/ truncation manifested within a persephin protein itself would be predicted to adversely alter its biologically active 3-dimensional conformation, and therefore, the antigenic/binding site itself, without requiring undue experimentation to determine otherwise.

Claim Rejections - 35 U.S.C. § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 32-38 are rejected under 35 U.S.C. 102(e) as being anticipated by Johnson et al (U.S. Patent 6,090,778).

Johnson et al. teach antibodies and a method of preparing antibodies to neurturin, which is a persephin/neurturin family member that inherently *comprise* "an oligopeptide that is part of the persephin polypeptide" (e.g., see Figure 15 of the instant application) at "amino acid sequences... conserved within the GDNF/neurturin/ persephin family" (i.e., column 27, lines 59-

63; column 44; Figure 5; as it relates to claims 35-36 & 38), and therefore, inherently are "*capable of* reacting with a persephin polypeptide..." (i.e., as it relates to claims 32, 35-36 & 38). In that these shared epitopes are reasonably also "hydrophilic" (e.g., see column 27, line 55-58), the limitations of claim 37 are anticipated. In that '778 (columns 27-28) teach polyclonal antibodies, as well as monoclonal antibodies, which further reasonably are "capable of reacting with a persephin polypeptide with about 80% or greater identity to SEQ ID NO:221" at these regions conserved within the GDNF/neurturin family, as indicated in Figure 5 of '778, and therefore, also are "conserved... [within the] GDNF/ neurturin/persephin family", the limitations of claims 32-34 are further met.

Information Disclosure Statement

6. The information disclosure statement filed 6/23/00 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because no copy of the Sloan reference was provided in the instant or parent application. It has been placed in the application file, but the information referred to therein has not been considered as to the merits for this crossed-out reference. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 C(1).

Conclusion

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Thursday, and alternate Fridays from 8:30 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert C. Hayes, Ph.D.
October 16, 2003